CASE STUDY

Successful treatment of POEMS syndrome in a young male with stem cell transplantation

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Abstract

POEMs syndrome is a rare paraneoplastic disorder related to plasma cell dyscrasia. The present study deals with an unusual case of POEMs syndrome in a young male who came with ascending demyelinating polyneuropathy, resulting in complete quadriparesis. The diagnosis was based on clinical findings of gynecomastia, hyperpigmentation and hypertrichosis of skin and lymphadenitis. Detailed laboratory investigations and imaging confirmed POEMS syndrome. In view of the rapidly progressing polyneuropathy, the patient was treated with chemotherapy followed by stem cell transplantation. The patient recovered completely after the treatment.

Keywords: POEMS, osteosclerotic myeloma, Crow-Fukase, Takatsuki disease

Case report

A 24-year-old male presented with acute onset lower limb weakness for three days followed by subsequent involvement of upper limbs. He had earlier undergone radiotherapy for right iliac bone plasmacytoma (Fig. 1) and was declared to be cured. On examination, the patient was afebrile and had wasting of bilateral masseter and temporalis muscles. He had bilateral gynecomastia, hyperpigmentation over chest wall and lower limbs, and enlarged axillary and iliac lymph nodes. His higher mental functions were normal on CNS examination. Right pupil was semi dilated with preserved extraocular movements and light reflex. Power in lower limbs was 0/5 and hand grip was weak. The deep tendon reflexes were absent in lower limbs and planters were mute. He had hypotonia in all the limbs. Bulbar muscles and other cranial nerves were normal. Other systemic examinations were normal. Fundus examination revealed right eye papilloedema. Lab findings revealed Hb 10.9 gm%, WBC 4800 /cmm, platelet count 4.63 lac/cmm, and ESR 80 mm/1hr. LFT and RFT were normal. In view of lower motor neuron quadriparesis, clinical diagnosis of acute inflammatory demyelinating polyneuropathy (AIDP) was suspected and nerve conduction velocity was performed. The test showed demyelinating neuropathy in upper limbs and axonal neuropathy in lower limbs. CSF examination was normal. The MRI of pelvis ruled out progression of plasmacytoma. His lymph node biopsy showed reactive hyperplasia and there was no malignancy or lymphoma.

In view of plasmacytoma, polyneuropathy and skin changes of lower limb, a diagnosis of POEMs syndrome was considered. His blood examination revealed β2 microglobulin 3.07 mg/dL (0.81-2.19), IgG 2010 mg/dL, (751-1500). Free kappa 40 mg/litre (3.3-9.4). Free lambda 61.34 mg/litre (5.71-26.3), and ratio 0.65 (0.26-1.65), Serum electrophoresis showed M-band, estradiol E2 101 (11-44) pg/ml, and testosterone 130 (142-923) ng/dl. The patient was initiated with chemotherapy with bortezomib 2 mg, cyclophosphamide 500 mg and dexamethasone. He underwent stem cell transplantation after 4 cycles of chemotherapy. His lower limbs power improved gradually to grade V and he was able to walk without support.

Discussion

POEMS syndrome, also known as osteosclerotic myeloma, Crow-Fukase syndrome or Takatsuki disease, is a rare paraneoplastic disorder related to plasma cell dyscrasias. The current case study discusses an atypical presentation of POEMS syndrome in a young male, as the classical case is frequently seen in 5th or 6th decades of life. It is characterized by the presence of ascending symmetrical demyelinating polyneuropathy and a monoclonal plasma cell disorder showing M band (M).

Fig. 1: Right iliac bone plasmacytoma

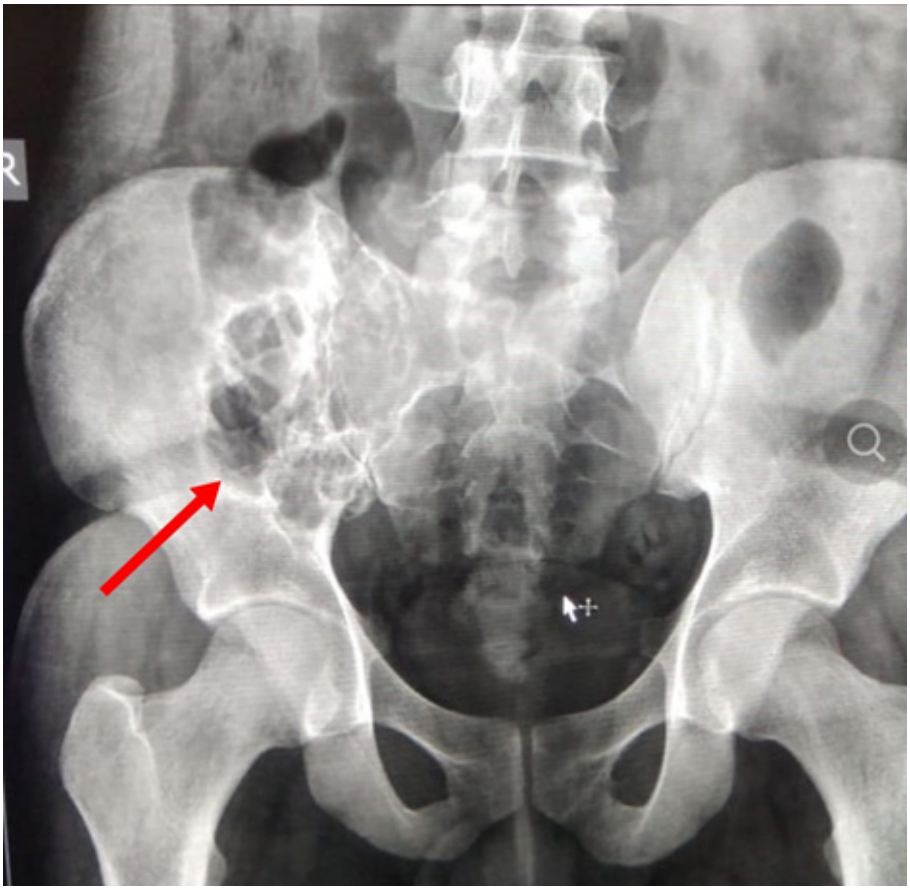
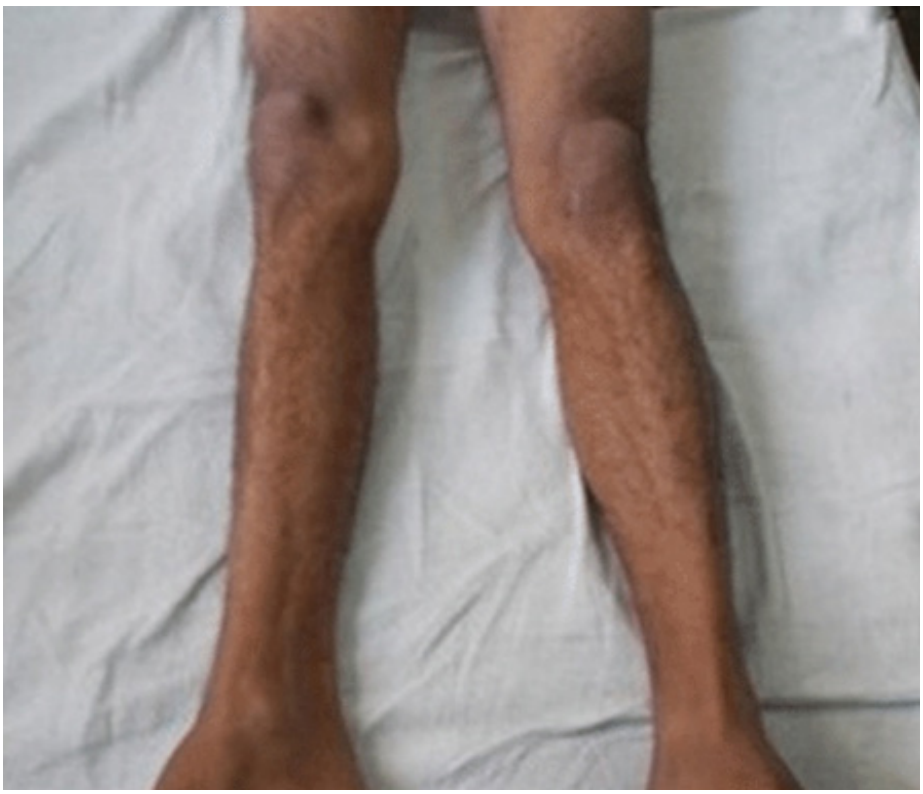


Fig. 2: Skin changes in the lower limbs



The other features include organomegaly, endocrinopathy, papilledema, effusion, ascites and thrombocytosis. Most of the patients have sclerotic bone lesions or Castleman's disease. The patient may not have all clinical features. and early recognition of the condition is essential to reduce morbidity. In order to diagnose POEMS syndrome, both the mandatory major criteria (i.e. demyelinating polyneuropathy and a monoclonal plasma cell disorder) should be present. Amongst the minor criteria, the patient had reactive lymphadenitis (organomegaly) and endocrinopathy in the form of gynecomastia, He also had skin changes of hypertrichosis and hyperpigmentation. The fundus examination revealed papilledema.

The usual treatments of demyelination polyneuropathy such as intravenous gamma globulin, plasmapheresis and azathioprine are not effective in POEMS syndrome. The mainstay of therapy includes irradiation, corticosteroids, and high-dose chemotherapy with peripheral blood stem cell transplantation. Association of plasma cell dyscrasias and peripheral neuropathy was well recognized in early 1950.[1] The patients of osteosclerotic myeloma were known to have features like skin pigmentation and lymphadenopathy. Bardwick in 1980 coined the term 'POEMS' to represent polyneuropathy (P) organomegaly (O), endocrinopathy (E) M protein (M) and skin changes (S).[2] However, the prevalence and the etiology of the disease is unknown. It is more common in Japanese people and has also been observed in European, African and Asian populations.[3] Though the presence of Lambda light chains has been implicated to be the cause of pathogenesis, they are not detected in the deposition. Antibodies of human herpesvirus (HHV-8) were reported in 78% of the patients of POEMS syndrome.[4] The most relevant factor of the syndrome is vascular endothelial growth factor (VEGF), which becomes normal with successful therapy.[5,6] VEGF is responsible for increase in vascular permeability and is an important factor for angiogenesis and osteogenesis.[7] VEGF is also expressed in osteoblasts and bone marrow, and hence it may play an important role in osteoblasts differentiation. In addition, the growth factor is secreted by plasma cells and platelets and is supposedly responsible for organomegaly, skin lesions and edema.[8,9] The patients also demonstrate high levels of IL-1β, TNF-α and IL-6 than those with multiple myeloma.[10]

Since **polyneuropathy** is a dominant clinical picture, the presentation includes symptoms like paresthesia, and distal to proximal weakness of gradual onset. Severe weakness occurs in more than half of the patients. The current patient had a complete quadriparesis and was wheel chair confined. The polyneuropathy was predominantly motor in nature and marked slowing of nerve conduction velocity was observed. The nerve biopsy in POEMS syndrome demonstrates a combination of degeneration and demyelination. However, it shows myeloid deposition, characterized by severe endoneural edema.

Organomegaly: It is often seen in the form of hepatomegaly, splenomegaly or lymphadenopathy. About 30% of the patients with POEMS syndrome has documented Castleman disease and the association is well recognized.[4] The present patient had reactive hyperplasia.

Endocrinopathy: Diabetic mellitus and gonadal dysfunction are the most common endocrinopathies. The current patient had gynecomastia. Other features noted are adrenocortical insufficiency and hypothyroidism. Endocrine glands appear to be normal in patients with necropsy.[6]

The plasma cell dyscrasia: The responsible monoclonal protein is not large and can be missed on serum protein electrophoresis in one third of patients if immunofixation is not performed. The serum immunoglobulin free light chain assay and immunofixation of urine are helpful to detect monoclonal lambda pattern. The bone marrow biopsy of iliac crest may not show clonal plasma cell infiltrate.

Nearly 50-90% of the patients demonstrate skin changes such as hyperpigmentation, and coarse longer and black hair over extremities. The current patient also demonstrated these manifestations (Fig. 2). Other skin changes include plethora or acrocyanosis, skin thickening like scleroderma and white nails with clubbing.[11,12] Osteosclerotic bone lesions are seen in 95% of patients and around 50% have a solitary sclerotic lesion.

Cyclophosphamide along with prednisolone can result in clinical improvement in 40% of the patients and can be used as a bridge therapy, while waiting for peripheral blood stem cell transplantation.[3,13] Many patients with POEMS syndrome are responsive to melphalan and prednisolone. Melphalan should be avoided in patients who are considered for stem cell transplantation.

High-dose chemotherapy with peripheral blood stem cell transplant was considered for the current patient, as his neurological condition was rapidly deteriorating. Since

the patient was young and without any systemic disease or organ dysfunction, he was considered as an ideal candidate for autologous stem cell transplantation. Most of the patients treated with this regimen have taken months to years to demonstrate neurological improvement. The transplant-related mortality is higher (7.4%) in patient with POEMS than in multiple myeloma (2%).[14]

Conflicts of Interest

The authors declare that they have no conflict of interest.

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Citation

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